REMARKS

Preliminary Amendment

The examiner objected to the formal drawing submitted for Figure 2A in the preliminary amendment. The examiner stated that this formal drawing contains new matter. It is unclear what aspect of the figure that the examiner believes is new matter. It does appear that the lines representing the electron density are rather faint, but they are visible in the submitted figure. Applicants submit that the formal drawing does not contain new matter. Applicants request that the examiner originally filed paper copy of the figure in the priority applications and compare these to the formal drawning..

Rejections Under 35 U.S.C. §112, second paragraph

The examiner rejected previously pending claims 46 and 47 as indefinite. The examiner argued that there are different numbering schemes for human CD11b and that it is unclear whether the amino acid numbering in the claims refers to mature or immature CD11b.

It is applicants' position that the specification and claims as originally filed clearly define human CD11b and that the actual amino acid sequence need not be incorporated. The specification refers to the Ile at amino acid 332 as being in the context of full-length CD11b, i.e., CD11b that includes the signal sequence (see page 14, Table 2 and page 7, lines 22-27). As is also clear from the specification, the Ile amino acid 332 of CD11b recited in Table 2 refers to the Ile at amino acid 332 of the full-length human CD11b sequence. For example, the specification provides the following explanation at lines 23-26 of page 7:

> Note that the amino acid numbering in these examples corresponds to the mature protein. While the amino acid numbering in Tables 2 and 3 below refers to the numbering in the complete protein (including signal sequence). CD11b has a 16 amino acid signal sequence.

Thus, it is clear that CD11b amino acid 316 in the examples, which refer to mature CD11b, corresponds to amino acid 332 of full-length CD11b, i.e., CD11b that includes the 16 amino acid leader sequence.

The examiner argued that previously pending claim 47, which depended from previously pending claim 46, was indefinite. According to the examiner, claim 47 recited unmodified human CD11b and claim 46 recited modified CD11b Claims 46 and 47 have been cancelled, obviating this rejection.

In view of the forgoing, applicants respectfully request that the examiner withdraw the rejections under 35 U.S.C. §112, second paragraph.

Rejections Under 35 U.S.C. §112, first paragraph (written description)

The examiner rejected previously pending claim 50 as failing to meet the written description requirement. The examiner argued that the original specification and claims do not support the limitation "wherein the Ile at amino acid 189 is replaced by an amino acid other than Ile".

Presently pending claims 51-53 refer to SEQ ID NO:1. As the examiner points out, SEQ ID NO:1, which is shown in Figure 5, is the A domain of CD11b (amino acids 144-334 of full-length human CD11b). The present claims refer to the Ile at amino acid 189 of SEQ ID NO:1 and this amino acid residue clearly corresponds to the Ile at amino acid 332 of full-length CD11b (or amino acid 316 of mature CD11b). For example, the description of Figure 5 on page 7 of the specification states that "the invariant Ile (I316) is indicated by an arrow". As can be seen from Figure 5 and SEQ ID NO:1 the Ile indicated by the arrow is the Ile at position 189 of SEQ ID NO:1. Thus, the specification and Figure 5 clearly support the limitations of claims 51-53.

The examiner rejected previously pending claims 46-50 as failing to meet the written description requirement. The examiner stated that "Applicant is not in possession of a purified polypeptide comprising amino acids 144 to 332 of full-length human CD11b wherein the Ile at amino acid 332 has been replaced by an amino acid other than Ile."

The present claims refer to polypeptides comprising the amino acid sequence of SEQ ID NO:1 (amino acid 144 to 334 of full-length CD11b) having the Ile at amino acid 189 changed to an amino acid other than Ile. Applicants have described two working examples of the claimed polypeptides. First, the present specification describes the construction of a vector encoding a "variant A domain with a Ile to Gly change at residue 316 ($11bA^{I\rightarrow G}$)" (see page 7, line 29). As explained above, since the examples use the numbering of mature CD11b, $11bA^{I\rightarrow G}$ has an Ile to Gly change at amino acid 332 of full-length CD11b. The protein encoded by this vector was produced, purified and used in a number of studies. Second, a vector encoding mature CD11c with the same Ile to Gly change was also generated (see pages 11-13 of the specification). This vector was used to produce a mature, variant CD11b polypeptide which was then purified and used in a number of studies. The two different purified proteins were tested in ligand binding assays and compared to otherwise identical proteins not having the Ile to Gly modification. As shown in Figures 4A and 4b, these variant proteins having the Ile to Gly modification exhibited increased ligand binding affinity compared to the corresponding wild-type CD11b A domain or mature CD11b protein. As the specification explains, these experiments together with the detailed structural studies described in the application are evidence that the Ile at 332 is critical for maintaining the "closed" or low affinity conformation of CD11b. As the specification also explains, replacement of the this critical Ile with another amino acid allows CD11b (or the A domain of CD11b) to be in the "open" or high affinity conformation.

Given that the specification provides working examples of two species within the claims and given that the specification provides the amino acid sequence of the A domain of CD11b (amino acids 144 to 334 of full-length CD11b), it is applicants' position that the present claims meet the written description requirement.

Rejections Under 35 U.S.C. §112, first paragraph (enablement)

The examiner rejected previously pending claims 46-50 as not enabled. The examiner appears to base this rejection on the fact that the specification as filed did not include a recitation of the actual amino acid sequence of full-length human CD11. As discussed above, it is

applicants' position that the specification and claims as originally filed clearly define human CD11b and that the actual amino acid sequence need not be incorporated. The present claims refer to SEQ ID NO:1, the A domain of CD11b, and do not include a reference to the amino acid sequence of full-length CD11b. In any event, the amino acid sequence of full-length CD11b is well-known in the art. As the examiner points out, the sequence was published by Corbi et al. in 1988, more than 12 years before the priority date of this application. Prior to the priority date of the present application many, many publications, some of which are cited in the present application, described the production and purification of CD11b. Moreover, the present application provides a detailed description of the preparation of polypeptides within the claims. Given the extension prior art literature regarding the cloning and purification of CD11b and given the detailed description of the preparation of CD11b A domain variants in the present application, it is applicants' position that the present claims are enabled.

Rejections Under 35 U.S.C. §102

The examiner rejected previously pending claim 47 as anticipated by Corbi et al. (1988). Corbi et al. discloses unmodified CD11b. The present claims are drawn to polypeptides comprising "amino acids 144 to 332 of SEQ ID NO:21 wherein the Ile at amino acid 332 has been replaced by an amino acid other than Ile". Corbi et al. does not teach of suggest such polypeptides. Applicants respectfully request that this rejection under 35 U.S.C. §102(b) be withdrawn.

Conclusion

Applicants submit that the claims are in condition for allowance. Enclosed is a Petition for Extension of Time with the appropriate fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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